ORIGINAL ARTICLE

Low Levels of Exposure to Libby Amphibole Asbestos and Localized Pleural Thickening

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Objective: To explore the relationship between low levels of exposure to Libby amphibole asbestos (LAA) and pleural abnormalities, specifically localized pleural thickening (LPT). **Methods:** Three studies presenting the risks associated with quantitative LAA exposure estimates were reviewed, paying particular attention to lower exposure ranges. **Results:** Studies reviewed were conducted among workers exposed to LAA at mining and milling operations in Libby, Montana, and at a vermiculite processing facility in Marysville, Ohio, and community residents exposed to LAA from a vermiculite processing facility in Minneapolis, Minnesota. Pleural abnormalities were evaluated using radiographs. Despite differences in study populations and design, each study found that cumulative inhalation LAA exposure was associated with increased risk of LPT even at low levels of exposure. **Conclusions:** Inhalation exposure to LAA is associated with increased risk of LPT even at the lowest levels of exposure in each study.

Libby amphibole asbestos (LAA) is a mixture of amphibole fibers present in ore from the vermiculite mine near Libby, Montana.[1] Workers and community residents were exposed to LAA at the mining operations in Libby, Montana,[2,3] as well as at vermiculite processing facilities in Marysville, Ohio,[4,5] and Minneapolis, Minnesota.[6] Epidemiologic studies of exposed populations indicate that exposure to LAA is associated with increased risk of adverse health effects, including lung cancer, mesothelioma, nonmalignant respiratory disease, and noncancerous radiographic abnormalities.[2,3,5,7,8] One example of such a radiographic abnormality is pleural thickening, a condition in which the pleural lining around the lungs (visceral pleura) or along the chest wall and diaphragm (parietal pleura) thickens because of fibrosis and collagen deposits.[9] This thickening has been characterized as either localized pleural thickening (LPT) or diffuse pleural thickening (DPT), with diffuse thickening representing a health endpoint of greater severity. In the current (2000) International Labour Organization (ILO) classification, LPT is focal areas of pleural thickening of the parietal pleura along the chest wall in which the costophrenic angle (CPA) is not blunted, or on the diaphragm.[10] Localized pleural thickening has been found to be the most "sensitive" health endpoint, occurring sooner after exposure to LAA than to other radiographic outcomes.[11] Furthermore, LPT is of clinical and public health importance because it represents a pathologic change, and although evidence is mixed, some studies indicate that LPT may be associated with decrements in lung function[12–17] and chest pain.[18]

For context, previous studies have provided information on the background rate of LPT in the general population. It is important to note that "LPT" is a relatively recent definition, and some studies instead use the designation of discrete pleural plaques; LPT may include both pleural plaques and pleural thickening that do not involve blunting of the CPA.[10] Two studies among populations, with no reported asbestos exposure, reported a pleural abnormality prevalence of 1.2% (4 of 326)[19] and 0.2% (3 of 1422).[20] Estimates of pleural thickening prevalence have also been reported from nationally representative cross-sectional studies; these populations may include persons with occupational exposure to asbestos, leading to higher prevalence. In the National Health and Nutrition Examination I study (1971 to 1975), the prevalence of pleural thickening was 1.2%,[21] and 3.9% in the National Health and Nutrition Examination II study (1976 to 1980).[22] Finally, two studies reported prevalence of 2.3% to 2.35% in military populations.[23,24]

Three recent studies have used quantitative exposure estimates to evaluate the relationship between LAA exposure and risk of LPT. These include two studies of occupationally exposed cohorts—the study of workers exposed to LAA at the mining and milling facilities in Libby, Montana,[25] and the study of workers exposed while processing Libby vermiculite in the production of lawn care products at the O.M. Scott facility in Marysville, Ohio.[5] In each case, workers were exposed to vermiculite ore from the mine in Libby, Montana, which was contaminated with amphibole asbestos fibers. The third study was conducted not among workers, but among community residents living near the Western Minerals facility in Minneapolis, Minnesota, which also handled vermiculite ore mined in Libby, Montana, during the production of building products such as insulation and fireproofing materials.[26] Although each study evaluated the association between LAA exposure and increased risk of LPT, there were differences in the exposure scenario, study population and design, and analytic approach. The objective of this review is to compare these three studies and evaluate the overall conclusions on the risk of LPT at low levels of exposure to LAA.

METHODS

We searched the literature for publications that evaluated health effects of exposure to LAA (rather than other forms of asbestos) specifically. Studies were selected that (1) provided quantitative exposure information, (2) evaluated LPT according to ILO guidelines, and (3) had a well-defined population, allowing prevalence estimate calculations. This review focuses on the study population and methods, with emphasis on the approach taken to estimate exposure to LAA and evaluate LPT. There have been numerous studies of health effects after exposure to LAA in different populations and subpopulations. The focus of this review is LPT, as identified on radiographic examination in studies by Larson et al,[25] Rohs et al,[5] and Alexander et al.[26] These studies were selected for evaluation because they were of populations exposed to LAA specifically (as opposed to other forms of asbestos), and because they provided quantitative exposure estimates. The findings of these studies are summarized and compared, focusing on risk of LPT at the lower levels of exposure.

Other studies including those conducted among Libby, Montana, community residents (both workers and nonworkers) did not provide quantitative exposure estimates.[27,28] In other cases, earlier studies were not used[3,4,29] because updated reports were available with longer follow-up times and improved exposure estimates.

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RESULTS

Study Summaries

Workers in Libby, Montana[25]

The study by Larson et al[25] was conducted among occupationally exposed workers at the mining and milling facilities in Libby, Montana (Table 1). Participants were identified and recruited through the Agency for Toxic Substances and Disease Registry (ATSDR) screening program begun in 2000.[27] Anyone who had lived, worked, or played in Libby for 6 months or more before 1991 was eligible for the ATSDR program, but this analysis focuses on former vermiculite workers (*n* = 336). These workers had both occupational and nonoccupational (ie, take-home and background) exposures to LAA; nevertheless, quantitative exposure estimates only considered occupational exposures. Exposure estimates were based on work performed by the National Institute of Occupational Safety and Health to estimate cumulative fiber exposure up through 1981[29] along with work done by ATSDR to estimate exposure from the early 1980s until the Libby facility closure in 1990. Based on these sources, the median cumulative inhalation exposure in this study population was 3.6 fibers per cubic centimeter times years (fibers/cc-yr), with an interquartile range of 0.4 to 15.8 fibers/cc-yr. At the time of screening (2000 to 2001), the median time since hire was 29.4 (interquartile range: 25.6 to 39.3) years.

Participants were offered posterior–anterior (PA) chest radiographs; they were also offered spirometry evaluation for lung function and were asked about respiratory symptoms including shortness of breath, excessive cough, and chronic bronchitis. The chest radiographs were evaluated for pleural abnormalities (including LPT, DPT, and parenchymal abnormalities) using ILO 1980 guidelines.[30] Specifically, LPT was defined as "the presence of circumscribed plaque on the chest wall (as indicated on the International Labor Office form) or diaphragm without the presence of DPT or parenchymal abnormalities (ie, for analytical purposes, subjects with concomitant LPT and DPT were categorized as DPT)."[25] The evaluation was performed by two B-readers, with independent reading by a third B-reader if the two primary readers disagreed.

Almost one-half (46%) of the workers in this study had some form of pleural abnormality and 35% had LPT. Workers with LPT had a mean cumulative exposure of 32.7 and a median of 5.8 fibers/cc-yr, compared with 36.8 and 2.1 fibers/cc-yr for those without LPT.

Workers in Marysville, Ohio[5]

The study by Rohs et al[5] also evaluated workers occupationally exposed to LAA (Table 1),[5] at the O.M. Scott facility in Marysville, Ohio. Exposure to LAA was assumed to have occurred from 1963 to 1980 on the basis of company records. The Rohs et al[5] study population consisted of 280 workers with approximately two decades of health follow-up and radiographic assessments. Occupational exposures were estimated using work records, interviews, and industrial hygiene measurements as described in Lockey et al,[4] with exposure estimated separately pre- and post-1973, when major process changes in the production process were initiated.[5] Overall, the mean (standard deviation) cumulative inhalation LAA exposure was 2.48 (4.19) fibers/cc-yr, and ranged from 0.01 to 19.03 fibers/cc-yr. The median time since first hire was 37.9 years for those with pleural changes, and 31.0 years for those without.

The study participants (enrolled from an earlier health evaluation study of plant workers[4]) were contacted for follow-up and invited to receive a PA chest radiograph. Radiographs were evaluated for pleural abnormalities (LPT, DPT, and interstitial changes) using ILO 2000 guidelines[10]; LPT was defined as "thickening with or without calcification, excluding solitary costophrenic angle blunting." In contrast to the studies by Larson et al[25] and Alexander

TABLE 1. Summary of Three Studies Evaluating the Relationship Between Libby Amphibole Asbestos Exposure and Risk of Localized Pleural Thickening

	Libby, Montana Larson et al[25]	Marysville, Ohio Rohs et al[5]	Minneapolis, Minnesota Alexander et al[26]
Study population	Workers (*n* = 336)	Workers (*n* = 280)	Community residents (*n* = 461)
	93.2% male, median age 55.6 (IQR: 47.4– 65.8) yrs	94.3% male, mean age 59.1 (age range 44–87) yrs	52.3% male, median birth year 1951–1960 (19.3% born ≤1940; 18.4% born ≥1960)
Time of assessment	2000–2001	2004–2005	2001–2003
Health outcome	LPT evaluated by consensus of two B-readers, 1980 ILO guidelines	LPT evaluated by median of three B-readers, 2000 ILO guidelines	Pleural plaques* evaluated by consensus of two B-readers, 2000 ILO guidelines
Exposure assessment	1945–1993	1963–1980	1980–1989
	Industrial hygiene measurements and work history (JEM)	Industrial hygiene measurements and work history (JEM)	Emissions-based modeling and self-reported activities
Exposure levels	Median: 3.6 fibers/cc-yr (IQR: 0.4–15.8)	Mean (standard deviation): 2.48 fibers/cc-yr (4.19)	Median: 2.42 fibers/cc-yr (cases) and 0.59 fiber/cc-yr (noncases)
Analytic approach	Logistic regression, exposure treated as categorical (quartiles) and continuous (restricted cubic splines)	Logistic regression, exposure treated as categorical (quartiles)	Logistic regression, exposure treated as categorical and continuous (log-transform)
	Covariates: age, sex, smoking history, BMI, hire era	Covariates: age, sex, smoking history, BMI, hire era	Covariates: year of birth, sex, occupational asbestos exposure

*Radiographic abnormalities were evaluated together as a group, and LPT was not modeled separately. Nevertheless, in the lower exposure group, all 17 cases had pleural plaques (personal communication from Bruce Alexander, June 7, 2013).
BMI, body mass index; ILO, International Labour Organization; IQR, interquartile range; JEM; LPT, localized pleural thickening.

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et al,[26] all radiographs were evaluated by three primary B-readers; the median reading was used to classify positive readings.

Over one quarter (28.7%) of participants had pleural changes of any type; 22.9% ($n = 64$) exhibited only LPT, and 1.4% ($n = 4$) exhibited both LPT and interstitial changes. When restricting to those participants with no exposure to commercial asbestos (including amosite, chrysotile, and crocidolite), those with LPT ($n = 56$) had higher cumulative exposure (mean and median levels of 3.45 and 1.52 fibers/cc-yr), than those without radiographic abnormalities (mean and median levels of 1.55 and 0.62 fibers/cc-yr). Among these workers without other asbestos exposure, the prevalence of LPT increased across increasing quartiles of exposure (6.7%, 18.6%, 28.8%, 40.7%) and the crude association with LPT was statistically significant in the third and fourth quartiles (odds ratios not given).

Community Residents in Minneapolis, Minnesota[26]

The study by Alexander et al[26] included individuals residing near the Western Minerals facility in Minneapolis, Minnesota, which processed Libby vermiculite from 1938 to 1989 (Table 1). Waste material was available to the community; thus, residents were exposed not only from emissions, but also via use of waste material in gardening or fill for driveways and yards, and through playing on the waste material. In 2000, the Minnesota Department of Health and ATSDR began the Northeast Minneapolis Community Vermiculite Investigation to characterize both occupational and nonoccupational exposures to LAA. Alexander et al[26] identified for their study the Northeast Minneapolis Community Vermiculite Investigation participants who were community members, had never worked at the facility, and had never lived with a facility worker ($n = 461$). To account for potential latency between exposure and outcome (ie, allow sufficient time for disease development), only residents exposed before 1980 were included. Participants were selected in stratified fashion to ensure a relatively wide range of exposure. Exposure groups were classified as intense intermittent exposure, long-term high ambient background exposure, and low ambient background exposure. As detailed in the publication by Adgate et al,[6] cumulative inhalation LAA exposure was estimated in units of fibers per cubic centimeter-month (fibers/cc-month) using information from two sources. Background exposure was estimated using modeled air concentrations from facility emissions, which spanned several orders of magnitude over the period of production. Activity-based exposure was estimated on the basis of self-reported contact activities (eg, direct contact with waste piles, using waste at home) in a Monte Carlo simulation, using distributions for duration, frequency, and range of fiber concentration; fiber concentrations were taken from activity reconstruction studies performed in Libby, Montana.[31,32]

Study participants received PA chest radiographs at a local contract medical clinic. Radiographs were evaluated for pleural abnormalities (pleural plaques, DPT, and parenchymal changes)

using ILO 2000 guidelines.[10] As in Larson et al,[25] radiographs were read by two B-readers, with a third B-reader if the two primary readers disagreed. Logistic regression models were used to evaluate the relationship between cumulative exposure to LAA and any pleural abnormality; results were not given for LPT or pleural plaques alone. Nevertheless, out of a total of 49 individuals with any pleural abnormality, 45 had pleural plaques, so that pleural plaques represent the majority of cases overall, and among the lower exposure group, all 17 cases of pleural abnormalities had pleural plaques (personal communication from Bruce Alexander, June 7, 2013). The definition of pleural plaques is similar to the definitions for LPT used in the other two studies evaluated, and is assumed to represent LPT for comparative purposes.

The overall prevalence of any pleural abnormality was 10.8%, and 9.8% ($n = 45$) had pleural plaques. Of the specific activities, playing on waste piles was also associated with increased risk. Of note, there were substantial numbers of pleural abnormalities even in the lowest exposure groups—for example, 17 among those with total cumulative exposure below the median level of 0.063 fiber/cc-yr (0.0523 fiber/cc-month).

Risk of LPT at Low Levels of Exposure

The study results regarding prevalence of LPT are summarized in Table 2. For each group, exposure was less than 1 fiber/cc-yr (upper end ranging from 0.28 to 0.63 fiber/cc-yr). The prevalence of LPT was highest in the study of Libby workers at 20%; the prevalence estimates for LPT in the Marysville study and LPT in the Minneapolis study were similar (6.7% and 7.4%, respectively).   [T2]

As noted earlier, previous studies have estimated the prevalence of pleural thickening to range from 0.2% (3 of 1422)[20] to 1.2% (4 of 326)[19] among non–asbestos-exposed populations, and from 1.2%[21] to 3.9%[22] in general population samples of adults aged 35 to 74 years (which may include those with occupational asbestos exposure). Thus, the estimated prevalence of LPT in the two occupational cohorts evaluated by Larson et al[25] and Rohs et al[5] is higher than any of the estimates of background rate of discrete pleural plaques in previous studies—although noting that LPT may comprise both discrete pleural plaques and pleural thickening that do not involve blunting of the CPA.[10] One possible factor that may affect prevalence of pleural abnormalities in asbestos-exposed populations is the age distribution of the population. The average ages among the two occupational cohorts described here were quite similar at 55[25] and 59 years[5]; in the community study by Alexander et al,[26] the median age was between 41 and 52 years.

Although quantitative exposure information was not available in the two studies of community residents in Libby, Montana, they also reported significant numbers of pleural abnormalities. The study   [AQ2]
by Peipins et al[27] was the first report on findings from the 2000 to 2001 evaluation of the ATSDR community cohort. Participants aged 18 years or more were offered lateral oblique (right and left) as well

TABLE 2. Three Studies Evaluating the Relationship Between Libby Amphibole Asbestos Exposure and Risk of Localized Pleural Thickening: Comparison Among Participants With Lower Exposure

	Libby, Montana	Marysville, Ohio*	Minneapolis, Minnesota†
Group	Quartile 1	Quartile 1	Quartiles 1 and 2
Exposure range	0 to <0.4 fiber/cc-yr	0.01–0.28 fiber/cc-yr	0 to <0.63 fiber/cc-yr
Prevalence	20% ($n = 17$ cases, 68 noncases)	6.7% ($n = 4$ cases, 55 noncases)*	7.4% ($n = 17$ cases, ~213 noncases)

*Note that the exposure range given is for the first quartile of exposure in the entire study population (ie, both with and without exposure to other, non-LAA, asbestos); the prevalence is calculated among those without exposure to other asbestos and may have a slightly different range of exposure. Nevertheless, it is likely to be very similar to that shown here, on the basis of similarity between ranges for the third and fourth quartiles of exposure as shown in the published article.

†Converted from 0 to less than 0.0523 fiber/cc-month. It is assumed that 230 (461/2) individuals comprise this group. As in Table 1, note that at the lower levels of exposure, all 17 cases had pleural plaques (personal communication from Bruce Alexander, June 7, 2013).

as PA radiographs, which were classified according to 1980 ILO guidelines.[30] Pleural abnormalities were defined as "(1) any unilateral or bilateral pleural calcification on the diaphragm, chest wall, or other site or (2) any unilateral or bilateral pleural thickening or plaque on the chest wall, diaphragm, or costophrenic angle site, consistent with asbestos-related pleural disease"; a positive result was recorded if noted by at least two of three B-readers. Overall, 17.8% of participants in the community cohort (including former workers) had a pleural abnormality, and prevalence was highest among former Libby workers (51.0%). Nevertheless, results were not provided for LPT specifically, or for individuals with lower potential for exposure. Weill et al[28] also evaluated pleural abnormalities among ATSDR screening cohort members using the same 2000 to 2001 radiographs and 1980 ILO guidelines.[30] In contrast to Peipins et al,[27] Weill et al[28] evaluated participants aged 25 years or more and only the frontal view radiographs were used. The two pleural outcomes were any DPT or CPA obliteration ("any two readers reporting any diffuse pleural thickening (DPT) or costophrenic angle obliteration (CAO), even if the readers did not agree on specifics" and pleural plaques ("any two readers reporting any diaphragm or wall, or other site plaques, even if the readers did not agree on specifics"). The prevalence of pleural abnormalities increased with increasing age and was (as expected) highest among workers from the Libby facility or other vermiculite or dusty occupations. Increased prevalence was also noted among those with household exposure (ie, lived with a vermiculite worker or worker in vermiculite or dusty occupation). Nevertheless, there were also abnormalities noted among those who did not have occupational or household exposures (ie, "environmental" exposure only, $n = 1894$). The prevalence of plaques ranged from 0.4%, among those 25 to 40 years, to 12.7%, among those 61 to 90 years of age. A total of 482 persons overall had a pleural abnormality excluding DPT, CPA obliteration, or profusion 1/0 or more. A total of 4065 members did not have any of the pleural abnormalities investigated, for a prevalence of approximately $(482/(482 + 4065)) = 10.6\%$.[28]

DISCUSSION

The three studies reviewed in this report, and all examined exposure to LAA in relation to LPT identified on radiographs. Nevertheless, there are important differences not only in the study populations but also in the ways that exposure and outcome were assessed, the analytic approach, and the conclusions. For each study, the average age of participants was around 50 to 60 years; nevertheless, the exact age distribution is difficult to compare because only Rohs et al[5] provide the age range for the study population, and Alexander et al[26] give birth year in categories rather than age at screening. The studies in occupationally exposed workers comprised more than 90% men,[5,25] whereas the study of community residents had almost equal numbers of men and women[26]; this could be important if sex affects susceptibility to, or the time course of, development of LPT. Of the two occupational studies, one[25] occurred in a setting where both occupational and nonoccupational exposures were very high, and nonoccupational exposures were not unaccounted for,[25] which may explain the higher rate of LPT in this population. In the other study,[5] exposures were generally lower and considered to be limited to the occupational setting. Nevertheless, in both cases, the exposure estimates for earlier years are quite uncertain; in the Libby facility, nearly all of the workers hired before 1960 were missing data on job and department.[8] In the Marysville facility, there were no fiber measurements before 1972.[33] Thus, in both cases it would be valuable to compare results from the whole cohort, to results among those hired during the time when more reliable exposure estimates were available. The third study, by Alexander et al,[26] was conducted among community residents (including a higher proportion of women compared with the other studies), and attempted to estimate exposure both from facility emissions and from specific activities.

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Nevertheless, exposure estimates relied on modeled emissions on the basis of very sparse data from the facility stacks and activity-based exposure reconstruction; thus, the authors estimate that the numerical uncertainty in exposure estimates could be an order of magnitude or more.[6]

Outcome ascertainment was also somewhat different between the three studies; although all three utilized PA chest radiographs, Alexander et al[26] and Rohs et al[5] used the 2000 version of the ILO guidelines to evaluate LPT, whereas Larson et al[25] used the 1980 version. Specifically, Larson et al[25] reported that LPT was defined as "the presence of circumscribed plaque on the chest wall (as indicated on the International Labor Office form) or diaphragm without the presence of DPT or parenchymal abnormalities." In contrast, the ILO 2000 guidelines define LPT in such a way that includes both pleural plaques and pleural thickening that do not involve blunting of the CPA between the rib cage and the diaphragm.[10] Thus, the 2000 guidelines may include a wider range of pleural abnormality compared with the more restrictive 1980 definition. Also with regards to outcome assessment, the consensus procedure differed across studies; in the study of community residents by Alexander et al,[26] the prevalence of pleural plaques observed by at least one reader was 16.2% ($n = 70$); however, this decreased to 9.8% ($n = 45$) when considering consensus readings only. Consensus information was not given in Rohs et al[5] or Larson et al.[25]

It is especially important to understand the health effects that result from exposure to LAA (particularly at low levels of exposure) because exposure may be widespread, and is not confined to the occupational setting. Records available from the W.R. Grace company indicate that from 1964 to 1990, more than 6 million tons of vermiculite concentrate was sent to more than 200 facilities such as the Western Minerals plant.[34] Beyond these occupational settings, Libby vermiculite was used in a wide range of consumer vermiculite products (including vermiculite attic insulation, drywall, horticultural soil additive, agricultural products, and laboratory packaging), creating the potential for widespread exposure. Several studies have attempted to characterize exposure from various nonoccupational routes. First, emissions from mining and processing operations may lead to ambient exposure in the surrounding area. Recent ambient air monitoring conducted by the Environmental Protection Agency in the Libby area detected asbestos fibers (albeit at low levels), even when there had been no disturbance of asbestos-contaminated material.[35] Levels detected ranged from 8×10^{-6} to 1.9×10^{-5} structures per cc of air (structures/cc)*. In the area surrounding the facility in Minneapolis, maximum ambient air concentrations ranged from 2.6×10^{-2} fibers/cc during peak production years (1936 to 1972) to 1.3×10^{-4} fibers/cc in more recent years (1999 to 2001).[36]

Studies from Libby have documented other routes for nonoccupational exposure, including take-home exposures for workers and their household contacts, playing with or handling vermiculite ore and waste rock, and traveling on or playing near the road leading to the vermiculite mine.[27,37] Exposure concentration estimates have been developed for some of these on the basis of activity reconstruction performed in Libby[31,32]; as described, Alexander et al[26] used these estimated ranges for the community study in Minneapolis as follows: "moving waste rock from plant 0.07–0.14 f/cc [fiber/cc], using waste rock at home 0.02–0.227 f/cc, installing or removing vermiculite insulation 0.142–0.568 f/cc, and playing in or around waste piles at the plant 0.14–1.72 f/cc." With regard to general population exposure to LAA, one route is through consumer products containing Libby vermiculite, as noted earlier. Studies have been performed to mimic VAI exposure scenarios that may be experienced

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*These measurements were performed using transmission electron microscopy (TEM), which yields results in units of structures per cc (structures/cc). In contrast, the three studies evaluated counted fibers in air samples using phase contrast and polarized light microscopy, which yields results in units of fibers per cc (fibers/cc).

by the average homeowner. For example, Ewing et al,[38] reported that the activity of cleaning items in an attic, where VAI is present, led to personal sample air concentrations of 1.54 fibers/cc; cleaning the storage area in such an attic led to concentrations of 2.87 fibers/cc.

CONCLUSIONS

This review compared three different studies, conducted in different populations with varying exposure contexts. Despite these differences, all three studies found an association between cumulative inhalation exposure to LAA and increased risk of LPT, and observed cases even at the lowest ranges of exposure for each study. Combining information across the three studies shows that the increased risk is present in a broad cross-section of the population—although the two occupational cohorts were largely male, the community study included both men and women, and a wider age range of participants. Further research is needed to understand how other population characteristics (eg, demographic factors, coexisting exposures, and health conditions) may impact risk of LPT after LAA exposure, and subsequent health outcomes. Another area for future research is to evaluate the exposure–response relationship between LAA and pleural abnormalities evaluated by high-resolution computed tomography, considered to be a more sensitive and specific tool than conventional radiographs[39]; high-resolution computed tomography can also provide insight into extent of pleural thickening, rather than solely presence or absence. Finally, further research is needed on health effects that are associated with LPT, including whether LPT can influence lung function controlling for the level of asbestos exposure. A more immediate implication for health care workers is that the presence of LPT and/or pleural plaques is "... an indication to monitor the patient over time for interstitial fibrosis."[39] The studies reviewed here show that even low levels of exposure to LAA are associated with substantial prevalence of LPT. If such exposure is known or suspected, health care providers should consider increased vigilance and monitoring.

ACKNOWLEDGMENTS

REFERENCES

1. Meeker GP, Bern AM, Brownfield IK, et al. The composition and morphology of amphiboles from the Rainy Creek complex, near Libby, Montana. *Am Mineral*. 2003;88:1955–1969.
2. Amandus HE, Althouse R, Morgan WKC, Sargent EN, Jones R. The morbidity and mortality of vermiculite miners and millers exposed to tremolite actinolite. Part 3. Radiographic findings. *Am J Ind Med*. 1987;11:27–37.
3. Mcdonald JC, Sebastien P, Armstrong B. Radiological survey of past and present vermiculite miners exposed to tremolite. *Br J Ind Med*. 1986;43: 445–449.
4. Lockey JE, Brooks SM, Jarabek AM, et al. Pulmonary changes after exposure to vermiculite contaminated with fibrous tremolite. *Am Rev Respir Dis*. 1984;129:952–958.
5. Rohs AM, Lockey JE, Dunning KK, et al. Low-level fiber-induced radiographic changes caused by Libby vermiculite. A 25-year follow-up study. *Am J Resp Crit Care*. 2008;177:630–637.
6. Adgate JL, Cho SJ, Alexander BH, et al. Modeling community asbestos exposure near a vermiculite processing facility: impact of human activities on cumulative exposure. *J Expo Sci Environ Epidemiol*. 2011;21:529–535.
7. Amandus HE, Wheeler R. The morbidity and mortality of vermiculite miners and millers exposed to tremolite actinolite. 2. Mortality. *Am J Ind Med*. 1987;11:15–26.
8. Sullivan PA. Vermiculite, respiratory disease, and asbestos exposure in Libby, Montana: update of a cohort mortality study. *Environ Health Perspect*. 2007;115:579–585.
9. Guidotti TL, Miller A, Christiani D, et al. Diagnosis and initial management of nonmalignant diseases related to asbestos. *Am J Resp Crit Care*. 2004;170:691–715.
10. ILO. *Guidelines for the Use of ILO International Classification of Radiographs of Pneumoconiosis. Revised Edition, 2000*. Geneva, Switzerland: International Labour Organization; 2000.
11. Larson TC, Meyer CA, Kapil V, et al. Workers with Libby amphibole exposure: retrospective identification and progression of radiographic changes. *Radiology*. 2010;255:924–933.
12. Bourbeau J, Ernst P, Chrome J, Armstrong B, Becklake MR. The relationship between respiratory impairment and asbestos-related pleural abnormality in an active work force. *Am Rev Respir Dis*. 1990;142:837–842.
13. Lillis R, Miller A, Godbold J, Chan E, Selikoff IJ. Radiographic abnormalities in asbestos insulators—effects of duration from onset of exposure and smoking - relationships of dyspnea with parencymal and pleural fibrosis. *Am J Ind Med*. 1991;20:1–15.
14. Jarvholm B, Sanden A. Pleural plaques and respiratory function. *Am J Ind Med*. 1986;10:419–426.
15. Schwartz DA, Fuortes LJ, Galvin JR, et al. Asbestos-induced pleural fibrosis and impaired lung function. *Am Rev Respir Dis*. 1990;141:321–326.
16. Miller A, Lilis R, Godbold J, Chan E, Selikoff IJ. Relationship of pulmonary function to radiographic interstitial fibrosis in 2,611 long-term asbestos insulators. An assessment of the International Labour Office profusion score. *Am Rev Respir Dis*. 1992;145:263–270.
17. Garcia-Closas M, Christiani DC. Asbestos-related diseases in construction carpenters. *Am J Ind Med*. 1995;27:115–125.
18. Mukherjee S, de Klerk N, Palmer LJ, Olsen NJ, Pang SC, Musk AW. Chest pain in asbestos-exposed individuals with benign pleural and parenchymal disease. *Am J Resp Crit Care*. 2000;162:1807–1811.
19. Anderson HA. Asbestosis among household contacts of asbestos factory workers. *Ann N Y Acad Sci*. 1979;330:387–399.
20. Castellan RM, Sanderson WT, Petersen MR. Prevalence of radiographic appearance of pneumoconiosis in an unexposed blue collar population—reply. *Am Rev Respir Dis*. 1985;132:1139–1139.
21. Rogan WJ, Gladen BC, Ragan NB, Anderson HA. US prevalence of occupational pleural thickening: a look at chest X-rays from the first National Health and Nutrition Examination Survey. *Am J Epidemiol*. 1987;126:893–900.
22. Rogan WJ, Ragan NB, Dinse GE. X-ray evidence of increased asbestos exposure in the US population from NHANES I and NHANES II, 1973–1978. *Cancer Causes Control*. 2000;11:441–449.
23. Miller JA, Zurlo JV. Asbestos plaques in a typical Veteran's hospital population. *Am J Ind Med*. 1996;30:726–729.
24. Muller JG, Bohnker BK, Philippi AF, Litow FK, Rudolph G, Hernandez JE. Trends in pleural radiographic findings in the Navy Asbestos Medical Surveillance Program (1990–1999). *Mil Med*. 2005;170:375–380.
25. Larson TC, Antao VC, Bove FJ, Cusack C. Association between cumulative fiber exposure and respiratory outcomes among Libby vermiculite workers. *J Occup Environ Med*. 2012;54:56–63.
26. Alexander BH, Raleigh KK, Johnson J, et al. Radiographic evidence of nonoccupational asbestos exposure from processing Libby vermiculite in Minneapolis, Minnesota. *Environ Health Perspect*. 2012;120:44–49.
27. Peipins LA, Lewin M, Campolucci S, et al. Radiographic abnormalities and exposure to asbestos-contaminated vermiculite in the community of Libby, Montana, USA. *Environ Health Perspect*. 2003;111:1753–1759.
28. Weill D, Dhillon G, Freyder L, Lefante J, Glindmeyer H. Lung function, radiological changes and exposure: analysis of ATSDR data from Libby, MT, USA. *Eur Respir J*. 2011;38:376–383.
29. Amandus HE, Wheeler R, Jankovic J, Tucker J. The morbidity and mortality of vermiculite miners and millers exposed to tremolite actinolite. 1. Exposure estimates. *Am J Ind Med*. 1987;11:1–14.
30. ILO. International Labour Office. International classification of radiographs of the pneumoconioses. *Med Radiogr Photogr*. 1981;57:2–17.
31. Weis CP. Amphibole mineral fibers in source materials in residential and commercial areas of Libby poses an imminent and substantial endangerment to public health. Memorandum from Christopher P. Weis, USEPA Senior Toxicologist/Science Support Coordinator, to Paul Peronard, USEPA On-Scene Coordinator for the Libby Asbestos Site. Environmental Protection Agency; 2001.
32. Weis CP. Fibrous amphibole contamination in soil and dust at multiple locations in Libby poses an imminent and substantial endangerment to public health: an addendum to my memorandum of May 10, 2000. Memorandum from Christopher P. Weis, USEPA Science Support Coordinator of the Libby Asbestos Site, to Paul Peronard, USEPA On-Scene Coordinator for the Libby Asbestos Site. Environmental Protection Agency; 2001.

33. Borton EK, Lemasters GK, Hilbert TJ, Lockey JE, Dunning KK, Rice CH. Exposure estimates for workers in a facility expanding Libby vermiculite: updated values and comparison with original 1980 values. *J Occup Environ Med.* 2012;54:1350–1358.

34. ATSDR. *Summary Report: Exposure to Asbestos-Containing Vermiculite From Libby, Montana, at 28 Processing Sites in the United States*. Atlanta, GA: Agency for Toxic Substances and Disease Registry; 2008.

35. EPA US. Summary of outdoor ambient air monitoring for asbestos at the Libby asbestos site, Libby, Montana (October 2006 to June 2008). Denver, CO. Available at http://www.epa.gov/libby/AmbientAirReportFinal09Feb2009.pdf. Published 2009. Accessed July 10, 2013.

36. Kelly J, Pratt GC, Johnson J, Messing RB. Community exposure to asbestos from a vermiculite exfoliation plant in NE Minneapolis. *Inhal Toxicol.* 2006;18:941–947.

37. ATSDR. *Toxicological Profile for Asbestos*. Atlanta, GA: US Department of Health and Human Services, Public Health Service; 2001.

38. Ewing WM, Hays SM, Hatfield R, Longo WE, Millette JR. Zonolite attic insulation exposure studies. *Int J Occup Environ Health.* 2010;16: 279–290.

39. American Thoracic Society. Diagnosis and initial management of nonmalignant diseases related to asbestos. *Am J Respir Crit Care Med.* 2004;170: 691–715.

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Author Queries

[AQ1]: Author: Please expand JEM.
[AQ2]: Author: Does the edited sentence "The study by Peipins et al . . . " convey the intended meaning? Please chck.
[AQ3]: Author: As per AMA guidelines, "gender" has been changed to "sex". Please check.
[AQ4]: Author: Please expand VAI.
[AQ5]: Author: Does the edited sentence "The authors thank the cohort participants . . . " convey the intended meaning? Please check.